

It is claimed:

1. A method of analyzing a population of oligomeric analyte molecules, wherein said molecules are composed of linked subunits of which at least 50% are uncharged, and are able to hybridize via Watson-Crick base pairing with a specific probe molecule which is a nucleic acid or charged nucleic acid analog, the method comprising:

(a) applying to a charge-bearing separation medium a mixture of (i) the population of analyte molecules and (ii) the probe molecule, under conditions such that complementary or near-complementary regions of the probe and at least one such analyte molecule are stably hybridized, thereby forming a mixture of species selected from probe-analyte duplex, single stranded analyte, single stranded probe, and combinations thereof, and

(b) separating said species within the medium.

2. The method of claim 1, wherein the nucleotide sequence of each analyte molecule is selected from the group consisting of a selected sequence, different length fragments of the selected sequence, internal deletion or insertion variants of the selected sequence, mutation variants of the selected sequence, and combinations thereof.

3. The method of claim 2, wherein said deletion, insertion or mutation variants contain at most one such deletion, insertion or mutation per 8 nucleotides of the selected sequence.

4. The method of claim 1, wherein the probe has a length and sequence such that its duplexes with different analyte molecules differ with respect to the presence, length or position of an unhybridized portion of the nucleic acid.

5. The method of claim 2, wherein the probe includes a sequence complementary to the selected sequence.

6. The method of claim 5, wherein the probe has a length equal to or no more than 25% greater than the selected sequence.

7. The method of claim 2, wherein the probe includes a sequence complementary to an N-1 deletion variant of the selected sequence.

8. The method of claim 7, wherein the probe has a length equal to said N-1 deletion variant of the selected sequence.

9. The method of claim 8, wherein said conditions are such that said probe hybridizes to only said N-1 deletion variant.

10. The method of claim 2, wherein variations in sequence or length among said analyte molecules occur within a given subregion of said selected sequence, and the probe is effective to stably hybridize to said subregion under the conditions of said analysis.

11. The method of claim 10, wherein the population contains analyte molecules which are N-1 deletion variants of the selected sequence, and the probe has a sequence and length sufficient to stably hybridize to each analyte molecule, under the conditions of said separating, at a region of the analyte molecule containing a deletion site.

12. The method of claim 10, wherein said subregion is at or near a terminus of said analyte molecule.

13. The method of claim 12, wherein said terminus is the 5' or 3' terminus, respectively, of the analyte molecule, and the probe comprises a labeling moiety at its 3' or 5' terminus, respectively.

14. The method of claim 13, wherein said labeling moiety is a fluorescent label.

15. The method of claim 1, wherein the charge bearing support is an ion exchange medium, and said separating of step (b) comprises passing an eluant through the medium.

16. The method of claim 1, wherein the charge bearing support is an electrophoresis medium, and said separating of step (b) comprises applying an electric field between opposing boundaries of the medium.

5        17. The method of claim 16, wherein the medium includes a superimposed pH gradient.

18. The method of claim 1, wherein the analyte molecules are composed of linked subunits of which at least 75% are uncharged.

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19. The method of claim 18, wherein all of said subunits are uncharged.

20. The method of claim 1, wherein the analyte molecules are selected from the group consisting of peptide nucleic acids, phosphotriester oligonucleotides,  
15 methylphosphonate oligonucleotides, morpholino oligomers, and chimeras of any member of this group with another member or with DNA, 2'-O-alkyl RNA, or 2'-O-allyl RNA.

21. The method of claim 20, wherein the analyte molecules are morpholino  
20 oligomers.

22. The method of claim 21, wherein said morpholino oligomers have intersubunit linkages selected from the group consisting of phosphoramidate and phosphorodiamidate.

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23. The method of claim 1, wherein the probe is selected from the group consisting of DNA, RNA, 2'-O-alkyl RNA, 2'-O-allyl RNA, phosphorothioate DNA, and chimeras thereof.

30        24. The method of claim 23, wherein the nucleic acid is DNA.

25. The method of claim 1, wherein the probe is labeled.

26. The method of claim 25, further comprising the step of detecting and quantitating a duplex of the labeled probe with at least one target analyte molecule in the population.

5        27. The method of claim 1, further comprising the step of isolating at least one said duplex.